Participant Information Sheet for Parent/Guardian

Mitochondrial DAMPs as mechanistic biomarkers in paediatric Crohn's disease

Mitochondrial DAMPs as mechanistic biomarkers of mucosal inflammation in paediatric Crohn's disease and Ulcerative Colitis (Mini-MUSIC)

Your child is being invited to take part in a research study. To help you decide whether to allow your child to take part, it is important for you to understand why the Mini-MUSIC study is being done, and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish. Contact us if there is anything that is not clear, or if you would like more information.

What is the background information about the study?

In Inflammatory Bowel Disease, Crohn's disease (CD) and Ulcerative Colitis (UC), one of the most important goals in treatment is complete mucosal healing of the gut. This means the return to a normal and healthy gut lining. For most IBD patients, full healing of the inflamed gut will lead to a return to normal bowel habit, energy levels, long-term remission and a better future.

Although we have good drugs for IBD, we do not currently have the best tests to accurately show how well these drugs are healing the gut. About 50% of patients who feel better on these drugs actually still have gut inflammation when examined with an endoscopy (an internal camera test). In other words, symptoms alone (for example, how you feel) are poor guides to whether the gut wall has healed or not.

We need better tests, beyond endoscopy, to monitor gut inflammation. Patients who continue treatments that are not fully healing the inflamed gut wall may be 'under-treated'. Other patients with complete healing of their gut and continue the drugs longer than required may be 'over-treated'.

What is the purpose of the study?

The Mini-MUSIC Study aims to investigate whether a new test that measures specific signals of inflammation can better inform IBD patients and their doctors about how their inflamed gut has healed in response to drug treatment.

In our previous research, we found that specific danger signals, called DAMPs (Damage-Associated Molecular Patterns), are released from a damaged cell's mitochondria within an inflamed gut. These danger signals are increased in patients with active IBD.

Mitochondria are the 'batteries' of human cells. They evolved from bacteria around 2-3 billion years ago, and so the mitochondria have many similarities with bacteria. This means that when our immune system encounters signals from damaged mitochondria, they can confuse them with bacteria, and become activated. Once activated, the immune system causes a prolonged inflammatory response. This inflammation damages the bowel wall.

Typically, doctors find out how well a drug treatment for active IBD has worked by asking the patient whether they feel better, and if their bowel symptoms have improved. They also check blood or stool tests (C-reactive protein and calprotectin) for signs of inflammation. The current evidence shows that such checks do not give the whole picture on whether the bowel wall has healed or not.

The best way to find out whether the bowel wall has healed is by carrying out an internal camera test to examine the bowel lining. In children and young people, unlike in adults, these internal camera tests are not done routinely as a monitoring test. These tests are invasive, involve general aesthetic, day admission to hospital and occasionally overnight hospital stays. Therefore it is important to look for better alternative tests of bowel wall healing.

In the Mini-MUSIC study, we will investigate the role of mitochondrial danger signals (DAMPs) as a marker for inflammation. We will measure these signals and assess how well they reflect the level of inflammation within the gut lining These will be measured both at the start and during medical treatment for active IBD.

If you choose for your child to take part, your child will continue to receive all standard NHS treatment by your child's IBD doctor. The Mini-MUSIC study will provide very close monitoring of your child's IBD over a 12-month period. We will monitor your child's reported symptoms, carry out the standard IBD blood and stool tests at each study visit, along with added research tests. All information gathered during your child's participation in the study will be given to your child's NHS doctor. Your child's NHS doctor may use this information to assist in your child's care and treatment decisions.

From the added samples obtained from your child, we will carry out further scientific studies to understand how the DAMPs signals activate inflammation in the gut in order to find new ways to block and stop this from happening. Doing so may find a new treatment in IBD. A similar study in adults, the MUSIC study, is currently being conducted in the UK. Results from both the paediatric Mini-MUSIC and the adult MUSIC study will help better understand and help patients with IBD across all age ranges.

Why has my child been invited to take part?

Your child has been asked to take part as they have IBD which is either newly diagnosed or not currently fully under control on their current medicines.

Does my child have to take part?

No, it is up to you and your child to decide whether or not to take part. If you decide to allow your child to take part you are still free to withdraw them at any time and without giving a reason. Deciding not to take part or withdrawing from the study will not affect the healthcare that your child receives, or your legal rights.

What will happen if my child takes part?

You and your child can take at least 24 hours to decide if you want to take part in the study. A member of the research team will give you this Information Sheet to read and an age-appropriate Information Sheet to your child. They will explain the study and give you and your child the opportunity to ask any questions. If you do decide to allow your child to take part you will both keep the Information Sheets. You, as your child's parent/guardian, will be asked to sign a consent form on your child's behalf. If applicable, your child may also be asked to provide assent depending on their age.

The study runs for 12 months and there are 3 study visits. The first study visit is at the start of the study. It is called the baseline visit. Your child will have a second study visit 3 months after baseline visit, and a final study visit at 12 months after baseline.

- Our research team will arrange a convenient time for your child to attend for each study visit. These appointments can coincide with your child's usual NHS visits (for example when you come to hospital for a routine clinic appointment to see your child's doctor, or during your child's drug infusion appointment, or a camera test appointment).

- We will ask you or your child (depending on age) to provide a short report of IBD symptoms at each study visit. This can be done in person at a clinic visit, by telephone, or by post.

- We will ask your child to provide a blood sample at each study visit. To minimise the number of needles, we will take your child's standard IBD blood tests at the same time as the research blood samples - a total of 25mls (5 teaspoons).

- We will ask your child to provide an optional saliva sample at each visit to examine the bacteria in the mouth (at baseline, 3 and 12 months).

- We will ask your child to provide an optional stool sample at each study visit. This is to measure the standard IBD stool tests, (calprotectin - a test for gut inflammation) and a research stool test to measure the gut bacteria. We can provide stool testing containers and special envelopes where you can choose to send to a dedicated research location at your convenience or bring with you to your child's study visit appointment.

- If your child's IBD doctor requires an ileo-colonoscopy or upper GI endoscopy to assess your child's IBD during the 12 month study period, we would ask that you inform the research team. We would want to record the results of this test into the study, and take research biopsy samples when this test is being done.

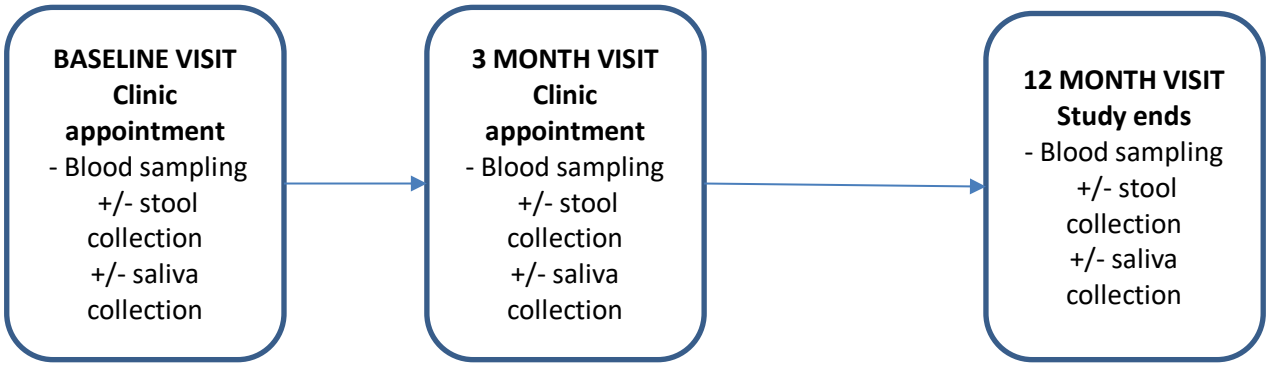
- If your child is admitted to hospital for further treatment of their IBD during the study period, we ask that you inform the research team. We will record the information of your child's IBD activity and all test results during this hospital stay. We may also approach you and your child again to give another research blood and stool sample, which will be taken at the same time as routine tests requested by your doctor in the hospital.

- If your child has a bowel operation as a result of their IBD, we ask that you inform the research team. We will ask your permission to take additional small samples of your child's bowel for research.

- We will ask for permission for our approved members of the research team to access your child's medical records to obtain study specific clinical information pertaining to their IBD only.

- The anonymised samples provided by your child and accompanying clinical data may be analysed to inform other related research projects.

Overview of involvement



What are the possible benefits of my child taking part?

Due to the nature of this study, your child's participation will mean that their IBD will be very closely monitored. It will be like having a 2nd pair of eyes on your child's condition running in parallel with their NHS IBD treatment.

By participating, the study information and test results will be given to your child's NHS IBD doctor. This information may help your child's doctor to make adjustments to improve your child's current IBD treatment.

Participation may give you and your child the opportunity to be more actively involved in their treatment and to engage more fully with the clinical team monitoring your child's IBD.

By putting you and your child at the forefront of research, participants may derive satisfaction from their inclusion in research intended to improve future IBD treatments and patient care.

We will offer reasonable travel expenses to cover additional hospital trips related to participating in this research study.

What are the possible disadvantages of my child taking part?

There is the possibility of pain or bruising from having a blood sample taken. We acknowledge the extra blood tests involved in participating in this study. For most IBD patients regular blood monitoring is usually necessary and we will endeavour to coincide the study blood tests with your child's regular clinic blood tests to minimise the number of samples.

We acknowledge the extra contribution of you and your child's personal time to attend the study visits. We will try to coincide these study visits with your child's regular IBD follow up appointments.

What if there are any problems?

If you have a concern about any aspect of this study please contact The Mini-MUSIC Research Team at miniMUSIC@ who will do their best to answer your questions.

What if my child no longer wants to participate?

You and your child are free to withdraw from the study at any point without giving a reason. In addition to this, they may also be withdrawn by the Investigator. If withdrawal occurs, the primary reason for withdrawal will be documented. If you and your child decide to withdraw your consent, no more information will be collected. All information you and your child gave us before leaving the study will still be used for the study. If your child withdraws from the study we would like to continue collecting information about your child's health from your child's hospital record. If you do not want this to happen for your child, tell us and we will stop.

If you and your child decide not to carry on with the study, the quality of care that your child receives will not be affected in any way.

Will my child taking part be kept confidential?

All the information we collect during the course of the research will be kept confidential and there are strict laws, which safeguard your child's privacy at every stage.

Your child's participation in this study will be recorded in their medical notes and their usual IBD doctor and GP will be informed.

The data collected in this study will be made anonymised and will not include any of your child's personal information (eg. name, date of birth). There is absolutely no way to be identified from these data. It will be kept confidential. We need to manage your child's records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data that we hold about your child.

Only members of the research team will be able to identify your child. They will abide by the Data Protection Act 2018 at all times and make sure your child's name, address, and any other information that would identify your child are removed from your child's medical information before it is given to any researchers.

The information held on computer will be kept secure, and all written information will be held in locked filing cabinets within research offices, under the direct responsibility of the Mini-MUSIC study doctor in your area.

Anonymised personal and clinical data obtained from the Mini-MUSIC study will be stored securely for a minimum of 5 years after the study finishes. Your child's biological samples (stool, saliva, blood and tissue) will be stored securely at the Centre for Inflammation Research, Queens Medical Research Institute, Edinburgh. These anonymised samples may be used as part of future research.

In order to monitor and audit the study we will ask your consent for responsible representatives from the sponsors and NHS institution to access your child's medical records and data collected during the study, where it is relevant to your child taking part in this research. The Sponsors are responsible for overall management of the study and providing insurance and indemnity.

How will we use information about your child?

We will need to use information from your child's medical records for this research project. Medical research is of more value if the researcher has information about the medical history of the person. We would like your permission to use and store information from your child's medical notes now, and possibly in the future as a follow up.

All information collected and stored will be kept strictly confidential. This information will be used to make sure relevant information is recorded for your child's care and to oversee the quality of the study. People will use this information to do the research or to check your child's records to make sure that the research details are being fully and correctly recorded. Your child's personal information - name and address, NHS number, your phone number, mail addresses will be used to contact you and your child about the research study. All identifying information will be removed before being given to anyone for their research – your child's data will have a code number instead. Only the research team and your healthcare team will be able to link your child's personal information to your child's research data.

Where can you find out more about how your child's information is used?

You can find out more about how we use your child's information:

- at www.hra.nhs.uk/information-about-patients/
- by asking one of the research team
- by sending an email to the mini-MUSIC team: miniMUSIC@

What will happen after my child has participated in the study?

The clinical data obtained from your child's 12 month study participation will be passed to your child's usual IBD doctor. Your child's doctor may adjust your child's medical treatment depending on the results of your child's tests over the course of the research study. After your child finishes the study their IBD care will continue as usual and be carried out by your child's IBD doctor.

Where will my child's research blood, stool and saliva samples be used?

The samples collected will be kept within the Gut Research Unit, Centre for Inflammation Research, Queens Medical Research Institute, University of Edinburgh and Wellcome Trust Clinical Research Facility, Western General Hospital under the oversight of the Lothian Gastroenterology Bioresource, University of Edinburgh and be processed every 2-3 months; or for certain experimental work, be used immediately in the Gut Research Unit, University of Edinburgh. Here, we will carry out new biomarker analysis from blood, stools and biopsies working together and in combination with our studies in Edinburgh.

At the end of the study, your child's anonymised samples that are not directly used by our research will be transferred to South East Scotland SAHSC BioResource under the guardianship of NHS Lothian or disposed in accordance to the Human Tissue Authority Code of Practice. Your child's anonymised samples and data saved from the study may be used by clinical, academic or commercial researchers, and maybe used in countries out with the United Kingdom undertaking similar research in partnership with our group. If you agree for your child to take part in this study, you will have the option to take part in future research using your child's data saved from this study.

What will happen to the results of the study?

It is important for our participants to be fully informed about the progress and results from this study. The overall results of the study will be published in medical journals but anonymously so results cannot be traced back to individuals. We will also provide fact sheets to communicate the most important study findings to IBD patients and general public.

The mini-MUSIC webpage for this study is where participants can read updates on the study's progress, results and the future publications that will come out from this work.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee. The committee has the responsibility for scrutinising all proposals for medical research on humans, has examined and raised no objections from the point of view of research ethics. This study has been checked and approved by Health and Social Care Research Ethics Committee A (HSC REC A). It is a requirement that your records in this research, be made available for scrutiny by monitors from NHS Lothian, whose role is to check that research is properly conducted and the interests of those taking part are adequately protected.

This study has been organised by the IBD Research Group in the University of Edinburgh and Royal Hospital for Children and Young People and sponsored by The University of Edinburgh and NHS Lothian. The study is funded by the Edinburgh Children's Hospital Charity.

The Lead Paediatric Investigator is Prof David C Wilson and Lead Research Fellow Dr. David Wands. The Chief Investigator is Dr. Gwo-tzer Ho.

Identifiable Data for future research

University of Edinburgh and NHS Lothian are the co-sponsors for this study based in Scotland. The co-sponsors are responsible for any identifiable information about your child for 5 years and are strictly governed by UK Policy Framework for Health and Social Care Research guidelines. In this study, we will use your Community Health Index (CHI) number, which uniquely identifies a patient within NHS in Scotland. Future information is provided in the accompanying leaflet Data Protection Information Sheet.

Researcher Contact Details

If you have any further questions about the study please contact Dr David Wands on david.wands4@ggc.scot.nhs.uk or Prof David C Wilson on +44 (0)131 312 0431 or email on: david.wilson@nhslothian.scot.nhs.uk

Independent Contact Details

If you would like to discuss this study with someone independent of the study please contact Dr Peter Gillett, Consultant Paediatric Gastroenterologist, Royal Hospital for Children and Young People on 0131 312 0431.

Complaints

If you wish to make a complaint about the study please contact

Patient Experience Team
2 – 4 Waterloo Place, Edinburgh, EH1 3EG, 0131 536 3370
feedback@nhslothian.scot.nhs.uk

Thank you for taking the time to read this Information Sheet and for considering your child's participation in this study